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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,605	10/11/2001	Grant McFadden	50082/015002	3282

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	9

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/976,605	Applicant(s) MCFADDEN ET AL.	
	Examiner Ulrike Winkler	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1-10,14,27-31,34-46 and 48-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,15-26,32,33 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election without traverse of Group 8 claims 11-13, 15-26, 32, 33 and 47 as the claims are drawn to SEQ ID NO: 5 in Paper No. 8 is acknowledged.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 5, is attached to the instant Office Action.

Drawings

The drawings are objected to, please see Notice of Draftsperson's Review attached to the instant Office Action. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide a sufficient written description for a "gene therapy vector" as it does not define how this vector differs from the naturally occurring virus which is capable of transferring the genetic material including the gp38 polypeptide into the host. The gene therapy vector is to provide a therapeutic benefit which can be interpreted to be a pharmaceutical composition or a drug; a drug by definition is an agent intentioned for the use in the diagnostics, mitigation, treatment, cure, or prevention of disease in humans or in other animals. Pharmaceutical therapies in the absence of *in vivo* clinical data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherent short half-life of the protein. (2) the protein may not reach the target area because, the protein may not be able to cross the mucosa or the protein may be absorbed by fluids, cells and tissues where the protein has no effect. (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of the treatment (see Vinyals et al., Gene Therapy, 1999; Thompson L., Human gene therapy harsh lessons, high hopes. FDA Consumer Magazine, 2000; Jackson et al., Journal of Virology, 2001). No working examples are provided which would provide sufficient guidance to allow one skilled in the art to practice the above embodiments of the invention with a reasonable expectation of success. Moreover, the nature of the invention and the state of prior art have not provided any reasonable expectation of success in using gene therapy vectors. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention with a reasonable expectation of success.

Claims 16-19 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification, while being enabling for SEQ ID NO: 5, does not reasonably provide enablement for the other homologous sequences that share 50-99% sequence identity on either nucleotide level. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification discloses the identification and characterization of a *Yatapoxvirus* protein with SEQ ID NO 6 and the corresponding nucleic acid sequence of SEQ ID NO:5. It would be undue burden for one of skill in the art to practice the claimed invention in terms of making all the homologous sequences from the disclosed sequences, because the specification provides no guidance as to the many different homologous sequences that can be produced. A 50%, 55%, 60%, 65%, 75%, 85%, 90% 95%, or 99% homology of SEQ ID NO:5 corresponds to a nucleotide difference of 517, 465, 413, 361, 258, 155, 103, 51 and 10 nucleotides. These nucleotide substitutions can be arranged contiguously or sparsely at different positions on a sequence. The state of the art is such that it cannot predict what substitution will result in significant structural or functional changes. The classic example of structural/functional differences is hemoglobin where a single amino acid substitution due to a single nucleotide change has significant consequences on the ability of the mutant hemoglobin to carry oxygen. A second example comes from a bacterial protease (Riffkin et al. Gene Vol. 167, 1995, pp 279-283), here a change in two nucleotides of the protease sequence results in the difference between

virulent and benign disease. This small difference does not only results in epitope differences but also results in changes to the thermostability, elastolytic and caseinolytic activity of the protease. There is no guidance in the specification to teach where the sequence should be substituted, and therefore, the functionality of the protein would be unpredictable. Moreover, one of skill in the art would not know which position of the substitution would retain the characteristics of a *Yatapoxvirus* polypeptide without undergoing extensive experimentation. Therefore, the instant specification does not provide enablement commensurate with the scope of the claims.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-13, 15, 19, 20, 21, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Neering et al. (Gene Bank Sequence, AF153912, direct submission, August 1999).

The instant invention is drawn to a "substantially pure" Yatapoxvirus nucleic acid sequence. "Substantially pure nucleic acid molecule" is defined in the specification as a nucleic acid molecule that is free of the components that naturally accompany it. "Immunomodulator" is

defined in the specification as an agent that induces an immunomodulatory effect or alteration as measured, for example, by an alteration of virulence in mutated viruses or a variety of immunoassays well known in the art. Based on the definition provided in the specification a peptide of sufficient length that will elicit an immune response such as producing an antibody (an altered level of immune function) would fall within the scope of the instantly claimed invention.

Neering et al. disclose a DNA sequence of a Tanapoxvirus fragment. In order to sequence the segment the DNA, the DNA needed to be purified. The standard sequences techniques requires the insertion of DNA into phage, growing the phage in bacteria (in a cell) and extracting the DNA for the sequencing reaction. A DNA sequence comprises both sense and antisense strands. The fragment is large enough to code for a protein that would elicit an immune response if injected into an animal. Therefore, the instant invention is anticipated by Neering et al.

Claims 11-13, 15, 19, 20, 21, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Amano et al. (Journal of General Virology, 1995; Gene Bank Sequence, D26580; AB015885).

The instant invention is drawn to a "substantially pure" Yatapoxvirus nucleic acid sequence. "Substantially pure nucleic acid molecule" is defined in the specification as a nucleic acid molecule that is free of the components that naturally accompany it. "Immunomodulator" is defined in the specification as an agent that induces an immunomodulatory effect or alteration as measured, for example, by an alteration of virulence in mutated viruses or a variety of

immunoassays well known in the art. Based on the definition provided in the specification a peptide of sufficient length that will elicit an immune response such as producing an antibody (an altered level of immune function) would fall within the scope of the instantly claimed invention.

Amano et al. disclose a DNA sequence of a Tanapoxvirus fragment. In order to sequence the segment the DNA, the DNA needed to be purified. The standard sequences techniques requires the insertion of DNA into phage, growing the phage in bacteria (in a cell) and extracting the DNA for the sequencing reaction. A DNA sequence is comprises both sense and antisense strands. The fragment is large enough to code for a protein that would elects an immune response if injected into an animal. Therefore, the instant invention is anticipated by Amano et al.

Claims 11 and 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (13th International Symposium of Poxvirus –Iridovirus, September 2-6, 2000.; Gene Bank Sequence, AJ293568).

The instant invention is drawn to a "substantially pure" Yatapoxvirus nucleic acid sequence, which is "substantially identical to" the nucleotide set out in SEQ ID NO:5 or the nucleic acid encoding the protein sequence of SEQ ID NO 6.

Lee et al. disclose a 1444575 bp DNA sequence of a Yaba-like disease virus a Yatapoxvirus. The DNA encodes proteins predicted to be involved in immune evasion. The sequence was submitted to Gene Bank Sequence, AJ293568 (July 13, 2000) is a 1444575 bp DNA submitted by the author of the poster presentation. Therefore, the instant invention is anticipated by Lee et al.

Claims 11-13, 15 and 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Paulose et al. (Micobial Pathogenisis, 1998, see IDS).

The instant invention is drawn to a "substantially pure" Yatapoxvirus nucleic acid sequence, which is "substantially identical to" the nucleotide set out in SEQ ID NO:5 or the nucleic acid encoding the protein sequence of SEQ ID NO 6.

Paulose et al. disclose the sequencing of the terminal amino acids (30 aa) from a 38 kDA expressed and secreted (identifiable signal sequence) protein of a Tanapoxvirus (see discussion last paragraph and material and methods). Therefore, the instant invention is anticipated by Paulose et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-13, 15, 19-22, 24-26, 32, 33 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neering et al. (Gene Bank Sequence, AF153912, direct submission, August 1999) in view of Panicali et al. (U.S. Pat. No. 5,656,465).

The instant invention is drawn to a "substantially pure" Yatapoxvirus nucleic acid sequence. "Substantially pure nucleic acid molecule" is defined in the specification as a nucleic acid molecule that is free of the components that naturally accompany it. "Immunomodulator" is defined in the specification as an agent that induces an immunomodulatory effect or alteration as measured, for example, by an alteration of virulence in mutated viruses or a variety of immunoassays well known in the art. Based on the definition provided in the specification a peptide of sufficient length that will elicit an immune response such as producing an antibody (an altered level of immune function) would fall within the scope of the instantly claimed invention.

Neering et al. disclose a DNA sequence of a Tanapoxvirus fragment. In order to sequence the segment the DNA needed to be purified. The standard sequences techniques requires the insertion of DNA into phage, growing the phage in bacteria (in a cell) and extracting the DNA for the sequencing reaction. A DNA sequence is comprises both sense and antisense strands. The fragment is large enough to code for a protein that would elects an immune response if injected into an animal. The reference does not teach inserting the DNA into a vector that is then inserted into a mammalian cell. The reference does not teach utilizing the sequences as a probe or formulating the probe into a kit.

Panicali et al. teach the use of poxviruses as gene delivery vectors.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize recombinant protein methods to produce products from known genes in order to obtain antigen for the purpose of using them in detection methods. The reference of Neering et al. teaches the DNA sequence from a Tanapoxvirus, while Panicali et al. teaches the construction of gene delivery vectors for the expression of genes in somatic cells using poxvirus. It would have been obvious to one of ordinary skill in the art at the time the invention was made to package the probe into a kit for diagnostic purposes. One having ordinary skill in the art would have been motivated to do package the required components into a kit for the sake of conveniently providing the reagents to unskilled personnel. Therefore, the inventions as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims limited to the SEQ ID NO: 5 or a nucleic acids that encodes SEQ ID NO 6 would be allowable.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER

7/14/03